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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,629	06/19/2001	Peter H. St. George-Hyslop	1034/1J800US1	3866

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	10

DATE MAILED: 03/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,629	ST. GEORGE-HYSLOP ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8-23 and 29-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed June 19, 2001, claims benefit to provisional application 60/212,534, filed June 20, 2000.

Claims 1-35 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-7, 24-28, filed February 21, 2003, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that examination of groups I and II should be done in the same application. Summarizing 35 USC 121 and Examiners reasons for the restriction requirement (pages 3-4), Applicants argue that a single inventive concept links both groups I and II. Specifically, Applicants note that the inventive concept of specific mutations in residues 670, 671 and 717 of APP_{695} is present in both the single transgenic animal of group I and the double transgenic of group II (page 4). Citing MPEP 806.05(c)II Applicants argue that the two groups should not be restricted because the related as subcombinations (pages 4-5). Further, Applicants argue that a search for group I requires the same class/subclass search and will identify relevant art in the non-patent literature relevant to the double transgenic. See Applicants' amendment, pages 3-5. Examiner notes that each the single transgenic and double transgenic have transgenes which comprise the specific mutations in residues 670, 671 and 7171 of APP_{695} however in the restriction groups I and II are not related as combination/subcombination. This is not found persuasive because the two groups are drawn to two materially different products. The relationship between the two instantly claimed products

is not simply A and B, but rather the manipulation of two distinct products by adding A or adding B. At most the two products could be considered as intermediate and final product, however single and double transgenic animals can be made through a variety methods and would not require this relationship. Further, in this relationship each the single transgenic and double transgenic would have separate and distinct properties and possible uses.

Additionally, it is noted that if group II was rejoined, the election of presenilin as he selected protein, and presenilin 1 L286V and M146L double mutant as the mutant is elected (page 6). Since groups I and II were not rejoined, the election of species is moot.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-35 are pending. Claims 8-23, 29-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Claims 1-7, 24-28 are currently under examination as they are drawn to a transgenic non-human mammal whose genome comprises a polynucleotide that encodes an amyloid precursor protein 695 transgene wherein the protein produced has the specific mutations in residues 670, 671 and 717 of APP_{695}.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Specifically, the specification provides a listing of all the references cited in the specification of this application, however a copy of references or a listing of references in the form of an IDS has not been provided for all the cited references. Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because of the following informalities: the specification has a Brief Description of the Drawings (page 7) and makes reference to figure 1 in other parts of the specification (see page 12, line 9 for example). However, no figures have been filed with the instant disclosure. See transmittal letter, section 4, filed June 19, 2001.

Clarification and appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 1 and 24 are vague and unclear in the recitation of "a heterologous amyloid precursor protein 695 (APP_{695}) polypeptide" because the metes and bounds of the claim are not clearly set forth. It is unclear if heterologous is in reference to the sequence relative to the mammal in which it is expressed, or just not naturally found in nature. Further, it appears that the protein comprises sequences that are mutants or polymorphisms, however it is unclear if the amino acids must be present because the claims do not recite that the sequences expressed represent the entire APP_{695} and may also comprise expressing fragments as encompassed by the term "polypeptide". The claims are indefinite because the metes and bounds of the nature of the polypeptide being expressed is not clearly set forth in the claims. Dependent claims are included in the basis of this rejection because they only define the type of mammal or the characteristic phenotype of the mammal without clearly setting forth what portions of the protein are necessary/required to affect the recited characteristic. More clearly setting forth the specific polynucleotide that is used or the polypeptide that is expressed would address the basis of the rejection.

Claim 6 is unclear in the recitation of "accelerated" because it is unclear what is considered accelerated. It is unclear if the original mammal must develop Alzheimer's Disease pathology for example a mouse of a (C3H x C57Bl6) x C57 background and in such a mouse the disease is accelerated, or if only the presences of the transgene is sufficient and the only thing

necessary for the development of the disease and acceleration is relative to a control mammal in which no disease develops.

Claim 7 is vague and unclear because the claim appears to encompass any transgenic mouse, as long as the mouse was part of its ancestry. The claim is not a product by process, and it is unclear if the claimed transgenic mouse must have the transgene set forth in claim 4, or if the claim encompasses any transgene as long as at one point in the

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 4-7, 24, 25, 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Sommer *et al.* (US Patent publication 2001/0016951 A1).

Claims 1, 2, 4-7, 24, 25, 27 and 28 are currently under examination as they are drawn to a transgenic non-human mammal whose genome comprises a polynucleotide that encodes an amyloid precursor protein 695 transgene wherein the protein produced has the specific mutations in residues 670, 671 and 717 of APP_{695}. The transgene specifically set forth as taught in the present specification with the three missense mutations is commonly known in the art as the Swedish mutation. Sommer *et al.* teach vectors comprising the APP_{695} as a transgene and

methods for making transgenic animals with said vector. Sommer *et al.* reduce to practice a transgenic mouse and the characterization of the transgenic mouse demonstrates that is possesses and demonstrates several characteristics of Alzheimer's Disease and that it would serve as an appropriate animal model to study the disease. Sommer *et al.* teach that the founder mice can be bred to provide offspring to derive a clonal line and to provide for a greater number of transgenic mice to study.

Claims 1, 2, 4-7, 24, 25, 27 and 28 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Sato *et al.* (US Patent 6,037,521).

Claims 1, 2, 4-7, 24, 25, 27 and 28 are currently under examination as they are drawn to a transgenic non-human mammal whose genome comprises a polynucleotide that encodes an amyloid precursor protein 695 transgene wherein the protein produced has the specific mutations in residues 670, 671 and 717 of APP_{695}. Sato *et al.* teach vectors comprising the APP_{695} as a transgene and methods for making transgenic animals with said vector. Sato *et al.* reduce to practice a transgenic mouse and the characterization of the transgenic mouse demonstrates that is possesses and demonstrates several characteristics of Alzheimer's Disease and that it would serve as an appropriate animal model to study the disease. Sato *et al.* teach that the founder mice can be bred to provide offspring to derive a clonal line and to provide for a greater number of transgenic mice to study.

Claims 1, 2, 4-7 and 24- 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Hsiao *et al.* (US Patent 6,509,515).

Claims 1, 2, 4-7, 24, 25, 27 and 28 are discussed above. Claim 26 encompasses the use of a prion promoter in the construction of transgene and transgenic mouse. Hsiao *et al.* teach to generate transgenic mice expressing various altered forms of APP known in the art including APP_{695}. with the Swedish mutation (see claim 1 and 2). Further, Hsiao et al. provide specific guidance to provide for the over expression of the transgene by make the construct under the control of the prion promoter (claim 1).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US Patent 5,455,169 (Mullan) describes the nucleic acid sequences for the Swedish mutation of APP, and it association with AD. Mullan propose that the disclosed sequence can be used if various contexts including the construction of transgenic animals, to study the role of APP in the pathology of AD.

US Patents: 5,672,805 (Neve), 6,262,335 (Hsiao *et al.*) and 6,175,057 (Mucke *et al.*) provide further evidence that transgenic mice can be made to express various forms of APP, including APP695, where the high expression of APP results in phenotypic characteristic seen in Alzheimer's Disease.

Conclusion

No claim is allowed. Claim 3 is free of the art of record. The art provides various genetic backgrounds for the resulting transgenic mice produced, however none specifically teach (C3H xC57BL6) x C57. Importantly, the art does teach that different genetic backgrounds provide the basis for differences in AD mouse models and differences in the severity and onset of the expected observed phenotypes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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